THE PATHOLOGY OF SUDDEN OPERATIVE DEATH*

By PAUL MICHAEL, M.D.
Oakland

DISCUSSION *by Paul H. Guttman, M. D., Sacramento; A. M. Moody, M. D., San Francisco; Jesse L. Carr, M. D., San Francisco.*

THE occasion of sudden operative death is, fortunately, a rare event in the course of surgical practice. The pathologist, situated as he is, may better be able to form a disinterested and unemotional opinion toward the solution of this problem when it occurs. Although a great deal of effort has been expended of late in evaluating the various factors, there is still much to learn before the final solution is reached.

The object of this paper is to endeavor to answer the following question: "What is it that happens to a patient appearing in relatively good health, with a normal blood pressure, normal heart action and no apparent pathologic derangement in the cardiac or respiratory systems, that causes a cataclysmic exitus on the operating table?" In answering the question, the scope of this paper must be qualified to include only those deaths occurring in the course of a general anesthesia involving the use of nitrous oxid and oxygen, ether, or both.

CAUSES OF SUDDEN OPERATIVE DEATHS

The following enumerated causes explain the great majority of deaths on the operating table:

1. Poor physical condition of the patient.
2. Improper technique in the administration of the anesthetic.
3. Impurities present in the anesthetic used.
4. Extreme loss of blood during the operation.
5. Asphyxiation.
6. Intracranial hemorrhage.
7. Acute hemorrhagic pancreatitis or hemorrhage into the pancreas.
8. Hemorrhage into the adrenals.
9. Coronary occlusion.
10. Embolism.
11. Fatal stimulation of the carotid sinus.
12. Persistent thymus or status lymphaticus.

Here we have twelve possible causes of death occurring in the course of an operation under a general anesthesia. Seven out of the twelve will commonly give us some organic characteristic picture at autopsy upon which we may make a diagnosis. These are: asphyxiation, embolism, intracranial hemorrhage, pancreatic hemorrhage, adrenal hemorrhage, coronary occlusion, and status lymphaticus or persistent thymus. In the remaining five the pathologist may be at a loss in making an anatomical diagnosis as to the cause of death.

The causes of poor physical condition of the patient are legion, and naturally cannot be enumerated. Such deaths may be the result of improper judgment or incorrect diagnosis, and should not be classed as due to the anesthesia. In this latter group we must remember that a death occurring during an abdominal laparotomy, when a coronary occlusion was present, cannot be attributed to the anesthetic alone.

COMMENT ON CAUSES OF SUDDEN OPERATIVE DEATHS

The following causes of death deserve a more detailed description of the anatomical findings and the causes ascribed to them:

1. *Asphyxiation.* — With rare exception, no matter the cause of asphyxiation, we have the following anatomical characteristics: cardiac dilatation, small petechial punctate hemorrhages over the visceral pleura and visceral pericardium, deeply bluish, red lungs showing marked edema and congestion, bilaterally and symmetrically scattered petechial hemorrhages in the basal ganglia.

2. *Intracranial Hemorrhage.*—Cerebral hemorrhage is not confined only to elderly people. We may also encounter it in younger patients, particularly in luetics and the thymic-constitutioned. The middle cerebral artery is the one principally involved, although hemorrhage of any of the Circle of Willis vessels may occur, with medullary pressure resulting. It must also be kept in mind that sudden death has been reported due to rupture of an aneurysm present within the cranial cavity.

3. *Hemorrhage Into the Pancreas.*—Acute hemorrhagic pancreatitis has been reported occurring during general anesthesia. None of the reported cases showed any symptoms referable to the pancreas prior to the anesthesia. The probable explanation of this is that duodenal contents, or irritating bile, regurgitates back into the pancreas. The pancreatic ferments then produce rapid destruction of the organ, causing death by shock from split-protein products.[1]

4. *Hemorrhage Into the Adrenals.*—Unilateral or bilateral hemorrhage into the adrenals during general anesthesia is sometimes seen as a cause of death. The whole adrenal gland may be involved, but usually the most marked hemorrhage occurs in the medulla. The rôle of the anesthesia in this hemorrhage is not well defined. The anatomical findings of cardiac dilatation and acute pulmonary congestion are found.

5. *Coronary Occlusion.* — Coronary occlusion may account for as high as 20 per cent of sudden deaths occurring in adults undergoing operation.[2] This figure does not include those patients incorrectly subjected to an abdominal laparotomy when a coronary artery obstruction is already present. The findings in these cases show that occlusion may occur at any point in the coronary arterial tree, but especially in the descending branch of the left coronary vessel. Acute passive congestion of all organs, especially the lungs, is seen at autopsy.

6. *Embolism.* — Pulmonary embolism presupposes a previous thrombosis, either due to tumor invasion of the vessel wall or to some previous vascular damage. Pulmonary infarction, then, rarely occurs on the operating table, although it is not infrequently seen as a postoperative complication. There are two special types of embolism,

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however, which merit additional consideration, namely, fat embolism and air embolism.

Fat embolism: Fat embolism may be due to endogenous or exogenous fat being introduced into the circulation. Endogenous fat embolism from the body itself may occur, especially during trauma or operations on the long bones. There may be an abnormal destruction of fat cells in the bone marrow, tearing of the venules in the Haversian canals of the bones, or increased internal pressure in the region of a fracture which may favor entrance of fat into the blood stream.[3]

Iodized oil is now frequently used as an opaque substance to fill cavities and occasionally may enter the blood stream. Due to abnormal pressure during injection, pathologic permeability of vessels, or injury to any organ during the injection, a disseminated fat embolism may occur. The mechanism of fat embolism may be explained on the basis of a physicochemical phenomenon. There is an alteration in the state of the existing fat in the blood stream leading to the formation of an emulsion. This naturally exists as a foreign body and may result in occlusion of small capillaries.

Fat emboli may lodge in the lungs, resulting in pulmonary embolism. The fat, however, may reach the lungs and do but a minimum amount of damage there, being forced through the lung capillaries into the left side of the heart and into the systemic circulation. From this point on, any organ or tissue may be involved. The fat is usually disseminated throughout the organ or tissue in small droplets which may be demonstrated by osmic acid or other fat stains. A paradoxical embolism due to a patent foramen ovale may occur, and this possibility must always be borne in mind.

Air embolism: Although man is particularly immune to embolism from air, such an event sometimes is seen. Two main types of air embolism are encountered; first, when a large quantity of air is injected into the venous system. At autopsy, the right heart is markedly dilated and contains a large amount of frothy blood. Death in these cases is usually the result of a mechanical obstruction ending in fatal auricular or ventricular fibrillation. The second type of fatal air embolism is encountered when air is accidently introduced into any one of the pulmonary arteries. Death erroneously attributed to "pleural shock" may be explained on this latter basis. Columns of air may disseminate through the systemic circulation, especially the brain. Air in the smaller arteries and arterioles leads to slowing of the blood stream, causing prestasis and stasis. Diapedesis takes place, resulting in small hemorrhagic points, progressing to occlusion and perivascular hemorrhage. Chase has shown that conglutination occurs during prestasis, while agglutination follows permanent stasis.[4] At autopsy, in these cases the brain shows cerebral edema, hyperemia and perivascular hemorrhages that may be cortical, subcortical, meningeal, or in the basal ganglia.

7. *Fatal Stimulation of the Carotid Sinus.*— This is a cause of death which has, until recently, been somewhat overlooked. Although no definite pathologic picture exists postmortem, abnormal stimulation of this sinus must be kept in mind as a possible factor. Death by pressure on the vagus nerve is probably explained as carotid sinus stimulation. The carotid sinus is located just behind the angle of the jaws. This bulb is a dilatation of the root of the internal carotid, which is somewhat delineated from the rest of the carotid artery by having a thinner wall and possessing an investment of sensory end-organs. These are connected to the brain by a branch of the glossopharyngeal nerve. In health the carotid sinus is in a state of fairly constant tonus. This tone increases or diminishes with the varying arterial pressure within it. The carotid sinus is also sensitive to other stimuli, such as pressure on the wall, stimulation of its nerve, or certain drugs. Morphin particularly may increase its response, resulting in hypotension and slowing of the heart.

Believing that the carotid sinus may sometimes be stimulated by certain anesthetics, a group of workers at the University of Pennsylvania [5] have recently shown that inhalant anesthesias have a stimulating effect upon the sinus. Nitrous oxid was found to cause such a stimulation. These workers used dogs, and employed 80 per cent nitrous oxid with 20 per cent oxygen. They reported no serious effects until the anesthetic had lasted at least twenty minutes. After this period certain dogs showed a respiratory arrest and circulatory collapse, similar to that observed in humans on the operating table. They believed that there was a toxic action of nitrous oxid probably associated with some personal idiosyncrasy, as this effect could not be repeated in all dogs. They reported no characteristic postmortem picture observed, although acute congestive failure was seen in all animals studied. The practical conclusions drawn by them from this study were:

1. In anesthesia, pressure on the carotid sinus must be avoided.

2. Ether vapor with nitrous oxid tends to offset the reaction.

3. In operative accidents, drugs are useless, artificial respiration being the best procedure.

8. *Persistent Thymus or the Thymicolymphatic Constitution.* — In 1930, Young and Turnbull,[6] reporting for the English Status Lymphaticus Investigation Committee on over six hundred autopsies, questioned the existence of a thymic diathesis. This conclusion fails to explain the importance of status lymphaticus, as much as the diametrically opposite belief that all sudden death may be explained on this basis. Between these two extremes are the more conservative pathologists who believe that many cases of sudden death may be thus explained. Douglas Symmers [7] has defined the thymicolymphatic constitution as a "combination of hereditary constitutional anomalies entering into which are usually certain peculiarities of configuration, with preservation or even hyperplasia of the thymus at an age when involution is to be expected—hyperplasia of the lymphoid cells of the spleen, intestines, and elsewhere; changes in the hair, hypoplasia of the vascular system, sometimes with congenital hypoplasia in the geni-

talia." An idea as to the prevalence of such a condition may be found in the Bellevue Hospital statistics. In a series of 4,000 autopsies, status lymphaticus was found in 249 cases, or in 6.2 per cent of the postmortem examinations. It was observed six times more frequently in males than in females. There were two main anatomical types: a true status lymphaticus, where the lymphoid tissues were hyperplastic and flourishing, and the recessive status lymphaticus, where the lymphoid tissues were atrophic but present microscopically.

Early in the study of this condition, sudden death, especially in small infants, was attributed to a mechanical obstruction of the trachea by an enlarged thymus. Anatomically, we now know that this belief is incorrect, as associated characteristics of this constitution include anatomic factors which may be predispositions of sudden death. For instance, this type of patient has a thin-walled vascular tree, especially in the brain. Hence there may be a personal idiosyncrasy for cerebral hemorrhage. These patients also have a hypoplastic aorta with small coronary vessels, hence they are predisposed to coronary arterial disease, interstitial fibrosis of the heart, and premature cardiac accidents. Graves's disease and persistent thymus are not infrequently related and may coexist in the same patient. A hyperplastic thymus is the rule in sudden death of patients suffering from Graves's disease. Finally, we know that asthmatics frequently belong in the thymico-lymphatic group with hypoplastic aorta, hypoplasia of the adrenal medulla, and lymphoid hyperplasia.[8,9,10] We, therefore, can associate with the persistent thymus the following predispositions to accident:

1. Cerebral hemorrhage.
2. Myocardial disease.
3. Graves's disease.
4. Asthma.

This last relationship has helped us form some conception as to the mechanism existing; that is, that the reaction between the anesthetic and the liberated nucleoproteins derived from the breaking down of tremendous numbers of lymphoid cells results in an anaphylactoid reaction. This is well borne out at autopsy when in these patients we notice large numbers of necroses occurring in the lymphoid areas, especially in the lymphoid follicles along the gastro-intestinal tract and in the thymus. As most of these split-protein products are liberated into the venous system, pulmonary edema is practically always found at autopsy.[10]

COMMENT ON FOUR CASES

During the past year, I have had the opportunity of studying four persons to determine the cause of death occurring under general anesthesia on the operating table. The first was in a female twenty-nine years of age, who died during a simple appendectomy soon after the abdomen was opened, and before any manipulative work was done. The second was a male, nineteen years of age, who succumbed at the end of an operation for hernioplasty. The third was a Chinese boy, sixteen years of age, who died during a tonsillectomy. The fourth was a male, fifty-five years of age, who expired during a thyroidectomy. In the female patient (first case) the recessive type of status lymphaticus with microscopic lymphoid hyperplasia was seen. There was an interstitial fibrosis of the heart with a coronary sclerosis out of all proportion to her age. In the second, third, and fourth, the thymus glands weighed 33, 38, and 80 grams, respectively. All of the male patients showed essentially the same anatomical findings, and the observations will be summarized as follows: The thymus in each instance was tremendously enlarged, and showed a marked hyperplasia with engorgement of the sinuses, and scattered focal necroses in the lymphoid elements. Pulmonary edema was marked in all, and there was some microscopic lymphoid cell infiltration of the lungs in the region of the hila. There was a moderate hypoplasia of the aorta with some coronary arterial disease, even in the young Chinese boy. The thyroid patient (Case 4) showed fairly marked medullary hypoplasia of the adrenals with definite eosinophilic cell infiltration. The entire lymphoid system, apart from the thymus, was hyperplastic in all cases, especially along the gastro-intestinal tract. Some of the lymphoid areas in this latter region showed focal necroses and areas of edema in the wall of the intestines.

There appears to be sufficient evidence from the above data that sudden death in many cases may safely be associated with the thymic constitution and its allergic interrelationship.

IN CONCLUSION

In conclusion, then, we see that sudden death under general anesthesia may occur and does occur regardless of the operation or the satisfactory physical condition of the patient. It does not reflect on the anesthetist, the surgeon, or the physician who conducts the preoperative examination. It is usually due to a combination of hereditary and constitutional anomalies, plus a personal idiosyncrasy which, with our present knowledge and armamentarium, may be impossible to ascertain.

There are a few practical suggestions gained from this study which may be of value:

1. Avoid pressure on the carotid sinus during anesthesia.
2. Make certain that a suitable physical examination has been made and that the necessary laboratory data are known.
3. Insist on a diligent examination on definitely known asthmatic children before submitting them to a general anesthesia.

434 Thirtieth Street.

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DISCUSSION

PAUL H. GUTTMAN, M. D. (605 Medico-Dental Building, Sacramento).—Doctor Michael has clearly pointed out that considerable controversy still exists on the question of status thymicolymphaticus. As the result of the careful studies of Hammar and, later, Boyd, conclusive data is presented which disproves the anatomical concept of status thymicolymphaticus. The size of the thymus and lymph nodes is dependent to a large extent upon the nutrition of the patient. In cases of sudden death from any cause, the weight of the thymus and size of the lymph nodes are large in well-nourished individuals. In those who suffer loss of weight as the result of prolonged illness, the weight of the thymus and lymph nodes decreases considerably. Failure to recognize these factors and the normal variation in the size of the thymus and lymph nodes has often resulted in the erroneous diagnosis of status thymicolymphaticus in cases in which the cause of death could not be determined.

It is often stated that degenerative changes are seen in the secondary follicles of the lymph nodes in status thymicolymphaticus. These changes are not constant and are frequently found in the course of normal involution of these glands and in toxic conditions unrelated to status thymicolymphaticus.

Although the anatomica concept of status thymicolymphaticus has suffered a blow as the result of the work of Hammar and Boyd, it is generally agreed that certain individuals who die as the result of trivial causes possess a constitutional inferiority which is not definable on an anatomical basis. Since we have no better terminology at the present time to classify this type of individual, it is well that the term "status thymicolymphaticus" is retained until this condition is better understood.

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A. M. MOODY, M. D. (St. Francis Hospital, San Francisco).—Doctor Michael has adequately covered the subject of sudden operative deaths in this paper. The first in his series of twelve causes, *i. e.*, "poor physical condition of the patient," will include many possible causes for sudden death when one adds to this anesthesia and varying amounts of surgical trauma and manipulation. The "constitutional inferiors" are quite apt to react abnormally during surgical procedures.

It should also be remembered that patients with diseased coronary arteries may die suddenly with or without occlusion of the arteries. The same may be said of those with fatty hearts.

Sudden operative deaths should be reduced considerably if the three practical suggestions offered by Doctor Michael in his conclusions are followed by all surgeons.

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JESSE L. CARR, M. D. (University of California Hospital, San Francisco).—In undertaking to discuss the pathology of sudden operative deaths, Doctor Michael has attempted a project which most of us evade. There are two main reasons for this. First, the cause of sudden operative death is frequently obscure, and second, it always involves the discussion of the status thymicolymphaticus. No one likes to attempt a study which he cannot complete with satisfaction to himself and to others involved, but even more does he hesitate undertaking a discussion of a subject about which there is great controversy, and following which there will be many a dubious one who will infer that the discusser does not know what he is talking about. This is especially true of any problem involving the thymic state. In reviewing the cases at the coroner's office in San Francisco, one would want readily to accept the other eleven good reasons that Doctor Michael lists as causes for sudden operative deaths; but he still will find the thymic complex staring him uncomfortably in the face.

To one who has seen any appreciable number of sudden fatalities on the operating table, there can be no doubt of a thymic status, and there can also be no question either about the fragility of people who have endured such a state. They do not, at autopsy, show adequate cytological causes for having died, but they do show consistently a hyperplasia of lymphoid elements wherever they may exist, and they also have a large thymus. It makes little difference whether or not one is willing to admit that the thymus has any lymphoid tissue in it, or whether it is an epithelial structure, the fact still remains that people with a thymus too large for their age and correlated with a lymphoid overgrowth or hyperplasia are consistently found dying suddenly and without further cytological changes upon being anesthetized.

Although Doctor Michael has only considered the type which has died following ether anesthesia, we would like to call attention to the fact that they die during operation whether or not ether is used. We have seen a death in this type of individual following local infiltration for cutaneous anesthesia, and another following cocainization of nasal mucous membranes, and even in operative cases in which no anesthetic was used. They are no doubt less resistant and more sensitive in their reaction to general anesthetics than are normal persons. But they are also more sensitive to other untoward stimuli as well.

Unfortunately, there is no clinical gauge or measure of the extent of this status in the living, excepting perhaps the thymic shadow and general anatomical topography in the young, so that it is necessarily hard to apprehend the disease. Certainly, however, it should be taught that status thymicolymphaticus does exist, and is one of the things which contribute to a sudden operative death.

Doctor Michael's other causes and their pathologic pictures are most interesting and soundly reviewed.

INJECTION OF SYMPATHETIC NERVOUS SYSTEM*

By PAUL G. FLOTHOW, M.D.
Seattle, Washington

DISCUSSION *by Charles F. McCuskey, M. D., Los Angeles.*

DESPITE all that has been done on diagnostic and therapeutic injections of the sympathetic nerves, there are still sympathetic operations being performed without adequate diagnostic measures to prognosticate the results.

There is little justification for unsuccessful operations on the sympathetic nervous system. This is particularly true of those operations employed for the relief of pain, in view of the fact that we have in hand a diagnostic measure that will determine definitely whether or not a given case will respond to operation.

By injection of the proper sympathetic nerves in cases of vascular insufficiency, it is a simple matter to determine quite definitely how much the blood supply to an extremity can be improved, and whether or not pain can be alleviated.

As far as we can ascertain, Von Gaza [1] was the first to inject the sympathetic nerves. He was followed by Swetlow,[2] White,[3] Flothow,[4] and others. The technique for injections of the sympathetic nerves is now quite well defined.

TECHNIQUE OF CERVICODORSAL SYMPATHETIC INJECTION

Swetlow's [2] technique will not be described. We use a technique illustrated to us by Lundy. For conditions pertaining to the head and upper ex-

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